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Osmolality of elemental and semi-elemental formulas supplemented with nonprotein energy supplements

L. Pereira-da-Silva,* M. Pitta-Grós Dias,† D. Virella* & M. Serelha*

*Neonatal Intensive Care Unit, Hospital Dona Estefânia, Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal; †Dietetic Service, Hospital Dona Estefânia, Lisbon, Portugal

Correspondence
Professor Luis Pereira-da-Silva,
Hospital Dona Estefânia,
Neonatal Intensive Care Unit,
Rua Jacinta Marto,
1169-045 Lisbon,
Portugal.
Tel.: +351 917235528
Fax: +351 217167203
E-mail: l.pereira.silva@netcabo.pt

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Abstract

Background Elemental and semi-elemental formulas are used to feed infants with short bowel syndrome, who may not be able to tolerate feeds of more than 310 mOsm kg^{-1}. The present study aimed to measure the osmolality of elemental and semi-elemental formulas at different concentrations, with and without the addition of non-protein energy supplements.

Methods The osmolality of one elemental and three semi-elemental formulas was measured by the freezing point depression method at concentrations of 10, 12, 14 and 16 g per 100 mL, with and without 10% or 20% of additional calories, in the form of glucose polymers and medium chain triglycerides. Inter-analysis and intra-analysis coefficients of variation of the measurements were less than 3.9%.

Results The mean osmolalities of formulas reconstituted up to 12 g per 100 mL did not exceed 305.3 mOsm kg^{-1}, even with added energy supplements. The mean osmolalities of formulas at 14 and 16 g per 100 mL, with or without added energy supplements varied between 205.8 and 421.6 mOsm kg^{-1}.

Conclusions A comprehensive list of elemental and semi-elemental formulas at different concentrations, enriched or not with calories, is made available. This will enable professionals to customize feeds with the optimum composition, without exceeding the osmolality suggested for infants with short bowel syndrome.

Conflict of interests, source of funding and authorship

The authors declare that they have no conflict of interest.

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LPS conceived and designed the study, performed osmometry and drafted the manuscript. MPGD prepared the formulas. DV analysed and interpreted the data. MS interpreted the data. All authors critically reviewed the content of paper and approved the final version submitted for publication.

Introduction

Infants suffering from short bowel syndrome (SBS) constitute a heterogeneous group, varying from preterm infants subjected to extensive bowel resection due to necrotizing enterocolitis, to full-term infants with severe gastrointestinal congenital abnormalities (Vanderhoof, 2003). Hence, it is difficult to design a single or a few standard formulas to suit the individual nutritional needs of every infant with SBS.

Semi-elemental formulas containing easily absorbable carbohydrates, or elemental free amino acid formulas, may be needed in infants with severe maldigestion and malabsorption (Vanderhoof, 2003; Goulet *et al.*, 2004). The more extensive the protein hydrolysis and the lower the molecular weight of carbohydrates, the higher is the osmolality of these formulas (Walker-Smith & Murch, 1999). High calorie density feeds may be achieved by concentrating the formulas or by adding nonprotein energy supplements such as glucose polymers (GP) and medium chain triglycerides (MCT) (Goulet, 1997; Hwang & Shulman, 2002; Romera *et al.*, 2004; O'Connor & Brennan, 2006). Both these strategies may provoke osmotic diarrhoea in infants with SBS due to their poor tolerance to high osmolar feeds. It has been postulated that infants with SBS may not tolerate enteral solutions with more than 310 mOsm kg^{-1} (Goulet *et al.*, 2004).

With the reconstitution of powdered formulas, osmolality is expected to change in proportion to the concentration as a linear function of molal units, the amount of solute per 1000 g of water (Anderson & Kennedy, 1986). It is also known that the addition of GP to formulas increases the osmolality according to their concentration and their molecular weight. By contrast, the particles of MCT exert a very low osmotically-active effect in solutions (Anderson & Kennedy, 1986; Jackson & Poskitt, 1991). Although the change in osmolality by addition of GP may be calculated mathematically (Anderson & Kennedy, 1986), it has not been determined to what extent osmolality is changed with the simultaneous addition of GP and MCT.

Several formulas have labels that do not provide information on osmolality, or osmolality is only listed for a standard dilution (Anderson & Kennedy, 1986). Other manufacturers only provide the calculated osmolarity values, which may be different from the actual measured osmolalities. In addition, it is difficult to compare the osmolality of similar formulas if their manufacturers use different methods of osmometry.

The aim of this descriptive study was to measure the osmolality of some commercially available elemental and semi-elemental formulas at different concentrations, with and without the addition of nonprotein energy supplements. This would provide professionals with a comprehensive list of energy and protein densities, helping to customize the feeds with the optimum composition without exceeding the osmolality limits suggested for infants with SBS.

Materials and methods

The elemental formula Neocate (SHS, Liverpool, UK) and the semi-elemental formulas Alfaré (Nestlé, Amsterdam, The Netherlands), Pepti-Junior (Nutrícia, Zoetermeer, The Netherlands) and Pregestimil (Mead-Johnson, Nijmegen, The Netherlands) were studied, throughout 2006. Table 1 shows the stated osmolarity and content of macronutrients of the formulas, according to the manufacturers' specifications for reconstitution.

The osmolality of these formulas was measured at a convenience set of similar concentrations: 10, 12, 14 and 16 g per 100 mL. At each concentration, the osmolality was also measured with a convenience supplementation of 10% or 20% of calories,

Table 1 Stated osmolarity and macronutrient content of the formulas for manufacturers' recommended reconstitution

Formula	Recommended reconstitution (g per 100 mL)	Stated osmolarity (mOsm L^{-1})	Protein	Carbohydrate	Fat
Alfaré	14.2	217	Extensively hydrolyzed: whey protein (100%)	Polysaccharides (86%), starch (11%), lactose residual (1%), others (2%)	Vegetable: MCT (47%)
Pepti Junior	12.9	180	Extensively hydrolyzed: whey protein (100%)	Polysaccharides (78%), maltose (11%), glucose (2%), others (11%)	Vegetable: MCT (50%), LCT (17%)
Pregestimil	13.2	300	Extensively hydrolyzed: casein (100%)	Polysaccharides (75%), dextrose (20%), others (5%)	Vegetable: MCT (55%)
Neocate	15	360	Free amino acids (100%)	Polysaccharides (81%), maltotriose (11%), maltose (7%), dextrose (1%)	Vegetable: LCT (95%), MCT (5%)

P : E, protein-to-energy; LCT, long chain triglyceride; MCT, medium chain triglyceride.

using powdered GP (Moducal; Mead-Johnson, Vansville, Indiana, USA; 1 g = 0.95 g maltodextrin) and MCT (MCT oil Module; SHS, Liverpool, UK; 1 mL = 0.95 g MCT), at a 1 : 1 glucose : lipid calorie ratio. Tables 2–5 show the energy density, the density of macronutrients, and the protein-to-energy (P : E) ratio provided by each formula.

All formulas were prepared by the same investigator according to a previously reported methodology (Pereira-da-Silva *et al.*, 2008).

Using a previously reported methodology (Pereira-da-Silva *et al.*, 2002), osmolality was measured by freezing point depression using the Osmomat 030 (Gonotec GmbH, Berlin, Germany), an automatic cryoscopic osmometer. Three samples of all analyzed formulas were measured in triplicate and measurements were compared to determine intra-assay and inter-assay coefficients of variation. All the samples were blindly measured by another investigator. Inter-analysis and intra-analysis coefficients of variation of the measurements were less than 3.9%.

Results

For each concentration, the formulas with higher measured osmolality were, in increasing order, Alfaré, Pepti Junior, Pregestimil and Neocate.

The mean osmolalities of the formulas at 10 and 12 g per 100 mL varied between 134.2 and 305.3 mOsm kg^{-1}, even with added energy supplements. As the concentration of formulas

Table 2 Formulas at 10 g per 100 mL, with and without nonprotein energy supplements: macronutrient content and measured osmolality

Formula	Concentration	Energy (kJ/kcal per 100 mL)	Protein (g per 100 mL)	P : E ratio g per 100 kJ/kcal	Carbohydrate (g per 100 mL)	Fat (g per 100 mL)	mOsm kg^{-1}
Alfaré	10 g per 100 mL	205.1/49.0	1.65	0.80/3.37	5.20	2.40	134.2
Pepti Junior	10 g per 100 mL	219.7/52.5	1.39	0.63/2.65	5.36	2.82	146.5
Pregestimil	10 g per 100 mL	214.3/51.2	1.40	0.65/2.73	5.10	2.80	217.1
Neocate	10 g per 100 mL	198.8/47.5	1.30	0.65/2.74	5.40	2.30	227.0
Alfaré	10 g per 100 mL + 10% calories	225.6/53.9	1.65	0.73/3.06	5.81	2.67	144.1
Pepti Junior	10 g per 100 mL + 10% calories	241.9/57.8	1.39	0.57/2.42	6.02	3.11	153.6
Pregestimil	10 g per 100 mL + 10% calories	235.6/56.3	1.40	0.59/2.49	5.74	3.08	223.4
Neocate	10 g per 100 mL + 10% calories	218.9/52.3	1.30	0.59/2.50	6.0	2.56	241.9
Alfaré	10 g per 100 mL + 20% calories	250.3/59.8	1.65	0.66/2.76	6.55	3.0	149.6
Pepti Junior	10 g per 100 mL + 20% calories	268.3/64.1	1.39	0.52/2.17	6.80	3.46	160.4
Pregestimil	10 g per 100 mL + 20% calories	261.6/62.5	1.40	0.54/2.24	6.51	3.43	233.8
Neocate	10 g per 100 mL + 20% calories	242.3/57.9	1.30	0.54/2.24	6.71	2.88	253.7

P : E, protein-to-energy.

Table 3 Formulas at 12 g per 100 mL, with and without nonprotein energy supplements: macronutrient content and measured osmolality

Formula	Concentration	Energy (kJ/kcal per 100 mL)	Protein (g per 100 mL)	P : E ratio g per 100 kJ/kcal	Carbohydrate (g per 100 mL)	Fat (g per 100 mL)	mOsm kg^{-1}
Alfaré	12 g per 100 mL	246.1/58.8	1.98	0.80/3.37	6.24	2.88	153.3
Pepti Junior	12 g per 100 mL	263.7/63.0	1.67	0.63/2.65	6.43	3.38	162.3
Pregestimil	12 g per 100 mL	257.0/61.4	1.68	0.65/2.73	6.12	3.36	256.7
Neocate	12 g per 100 mL	238.5/57.0	1.56	0.65/2.74	6.48	2.76	270.3
Alfaré	12 g per 100 mL + 10% calories	270.8/64.7	1.98	0.73/3.06	6.98	3.21	159.7
Pepti Junior	12 g per 100 mL + 10% calories	290.0/69.3	1.67	0.58/2.42	7.22	3.73	170.7
Pregestimil	12 g per 100 mL + 10% calories	282.9/67.6	1.68	0.59/2.49	6.89	3.70	260.3
Neocate	12 g per 100 mL + 10% calories	262.4/62.7	1.56	0.59/2.50	7.19	3.08	294.0
Alfaré	12 g per 100 mL + 20% calories	300.1/71.7	1.98	0.66/2.76	7.86	3.60	163.7
Pepti Junior	12 g per 100 mL + 20% calories	321.8/76.9	1.67	0.52/2.17	8.16	4.15	177.7
Pregestimil	12 g per 100 mL + 20% calories	313.5/74.9	1.68	0.54/2.24	7.81	4.11	271.3
Neocate	12 g per 100 mL + 20% calories	290.9/69.5	1.56	0.54/2.24	8.05	3.46	305.3

P : E, protein-to-energy.

Table 4 Formulas at 14 g per 100 mL, with and without nonprotein energy supplements: macronutrient content and measured osmolality

Formula	Concentration	Energy (kJ/kcal per 100 mL)	Protein (g per 100 mL)	P : E ratio g per 100 kJ/kcal	Carbohydrate (g per 100 mL)	Fat (g per 100 mL)	mOsm kg^{-1}
Alfaré	14 g per 100 mL	287.1/68.6	2.31	0.80/3.37	7.28	3.36	205.8
Pepti Junior	14 g per 100 mL	307.6/73.5	1.95	0.63/2.65	7.50	3.95	242.0
Pregestimil	14 g per 100 mL	300.1/71.7	1.96	0.65/2.73	7.14	3.92	313.3
Neocate	14 g per 100 mL	278.3/66.5	1.82	0.65/2.74	7.56	3.22	326.6
Alfaré	14 g per 100 mL + 10% calories	316.0/75.5	2.31	0.73/3.06	8.14	3.74	219.2
Pepti Junior	14 g per 100 mL + 10% calories	338.6/80.9	1.95	0.58/2.42	8.42	4.36	252.8
Pregestimil	14 g per 100 mL + 10% calories	330.2/78.9	1.96	0.59/2.49	8.04	4.32	330.8
Neocate	14 g per 100 mL + 10% calories	306.3/73.2	1.82	0.59/2.50	8.39	3.59	347.4
Alfaré	14 g per 100 mL + 20% calories	350.3/83.7	2.31	0.66/2.76	9.17	4.20	237.7
Pepti Junior	14 g per 100 mL + 20% calories	375.4/89.7	1.95	0.52/2.17	9.53	4.85	262.7
Pregestimil	14 g per 100 mL + 20% calories	366.2/87.5	1.96	0.54/2.49	9.11	4.80	337.0
Neocate	14 g per 100 mL + 20% calories	339.4/81.1	1.82	0.54/2.24	9.39	4.03	352.1

P : E, protein-to-energy.

increased up to 12 g per 100 mL, acceptable energy (up to 290 kJ (69.3 kcal) per 100 mL) and protein (up to 1.98 g per 100 mL) densities are achieved without exceeding 310 mOsm kg^{-1}, even in formulas enriched with energy supplements (Tables 2 and 3).

The mean osmolalities of formulas at 14 and 16 g per 100 mL, enriched or not enriched with energy supplements, varied between 205.8 and 421.6 mOsm kg^{-1}. The formulas Alfaré and Pepti Junior, even at concentration of 16 g per 100 mL with added energy supplements, did not exceed 310 mOsm kg^{-1}, with the exception of Pepti Junior at 16 g per 100 mL + 20% calories (Tables 4 and 5). By contrast, all the Pregestimil and Neocate formulas at concentrations ≥14 g per 100 mL exceeded 310 mOsm kg^{-1}, even without added energy supplements (Tables 4 and 5).

Discussion

Until evidence-based data is made available, the Committee on Nutrition of the American Academy of Pediatrics has recommended infant formulas with concentrations no greater than 400 mOsm kg^{-1} (American Academy of Pediatrics, Committee on Nutrition, 1976). However, Goulet *et al.* (2004) suggest that infants with SBS

Table 5 Formulas at 16 g per 100 mL, with and without nonprotein energy supplements: macronutrient content and measured osmolality

Formula	Concentration	Energy (kJ/kcal per 100 mL)	Protein (g per 100 mL)	P : E ratio g per 100 kJ/kcal	Carbohydrate (g per 100 mL)	Fat (g per 100 mL)	mOsm kg^{-1}
Alfaré	16 g per 100 mL	328.1/78.4	2.64	0.80/3.37	8.32	3.84	246.0
Pepti Junior	16 g per 100 mL	351.5/84.0	2.22	0.63/2.65	8.58	4.51	290.9
Pregestimil	16 g per 100 mL	342.8/81.9	2.24	0.65/2.73	8.16	4.48	378.0
Neocate	16 g per 100 mL	318.1/76.0	2.08	0.65/2.74	8.64	3.68	381.6
Alfaré	16 g per 100 mL + 10% calories	360.7/86.2	2.64	0.73/3.06	9.30	4.28	261.6
Pepti Junior	16 g per 100 mL + 10% calories	386.7/92.4	2.22	0.57/2.42	9.63	4.98	304.8
Pregestimil	16 g per 100 mL + 10% calories	377.1/90.1	2.24	0.59/2.49	9.18	4.94	408.3
Neocate	16 g per 100 mL + 10% calories	349.9/83.6	2.08	0.59/2.50	9.59	4.10	406.2
Alfaré	16 g per 100 mL + 20% calories	404.7/96.7	2.64	0.65/2.76	10.48	4.80	279.7
Pepti Junior	16 g per 100 mL + 20% calories	429.0/102.5	2.22	0.52/2.17	10.89	5.54	325.7
Pregestimil	16 g per 100 mL + 20% calories	418.1/99.9	2.24	0.54/2.24	10.41	5.48	427.7
Neocate	16 g per 100 mL + 20% calories	387.9/92.7	2.08	0.54/2.24	10.73	4.61	421.6

P : E, protein-to-energy.

may not tolerate enteral solutions exceeding 310 mOsm kg^{-1}. To the best of our knowledge, no evidence-based data have been published on this subject.

The degree of hydrolysis and the type of carbohydrates included in formulas have an important role in determining their osmolality. The higher the molecular weight of the carbohydrates, the lower is the osmotic pressure of a solution containing a given number of calories will be (e.g. the osmolality of a 20% solution of dextrose is 1110 mOsm L^{-1} and that of Caloreen, Nestlé Clinical Nutrition – GP is 240mOsmol L^{-1}) (Walker-Smith & Murch, 1999). This explains the higher osmolality of the analyzed semi-elemental formulas containing higher proportion of dextrose in relation to GP or starch (Table 1). Furthermore, the high osmolality of the analyzed elemental formula is mainly determined by the fact that the protein content is exclusively in the form of low molecular weight free amino acids (Walker-Smith & Murch, 1999).

Infants with SBS constitute a heterogeneous group. For example, a formula containing an energy density of 339 kJ (81 kcal) per 100 mL and a P : E ratio of 0.72–0.79 g per 100kJ (3–3.3 g per 100 kcal) may be needed for the catch-up growth of very low birth weight infants (Klein, 2002; Rigo & Senterre, 2006), whereas a formula containing 251–293 kJ (60–70 kcal) per 100 mL and a P : E ratio of 0.43–0.48 g per 100 kJ (1.8–2.0 g per 100 kcal) may be appropriate for term infants (Koletzko *et al.*, 2005). In addition, a wide range of digestive and absorptive capacities is observed in infants with SBS, depending on the length and function of the remaining intestine (Goulet *et al.*, 2004). Thus, the nutritional management should be planned on an individual basis (Vanderhoof, 2003; Goulet *et al.*, 2004).

Administration of restricted volumes of elemental or semi-elemental formulas with high energy density feeds is a possible strategy, whereas full enteral feeding is not achieved (Goulet, 1997; Hwang & Shulman, 2002). Low volume hypercaloric feeds may be provided by concentrating powdered formulas above the currently recommended concentration. By reducing the amount of added water, this method increases the level of all macro and micronutrients, resulting in a more balanced formulation (O'Connor & Brennan, 2006). Once the maximum levels of limiting nutrients are reached, energy modules, either carbohydrate or fat, may be added to the formula to further increase energy content alone (Goulet, 1997; Hwang & Shulman, 2002; Romera *et al.*, 2004; O'Connor & Brennan, 2006). In neonates, GP are preferred as a modular supplement because they are rapidly cleared from the stomach and absorbed (Costalos *et al.*, 1980). In cases of ileal resection, MCT may also be used as a modular supplement because they do not require the presence of bile acids for absorption (Thureen &

Hay, 2005), being absorbed to some extent from the stomach and duodenum, and rapidly hydrolyzed by pancreatic lipase, reaching the liver directly via portal circulation due to their water solubility (Bach & Babayan, 1982). In the present study, GP and MCT were added at appropriate glucose:lipid calorie ratio, considering that fat has a lower respiratory quotient, thereby reducing the risk of excessive carbon dioxide production caused by adding GP to the formulas (Walker-Smith & Murch, 1999). However, the addition of nonprotein supplements to standard formula has the undesirable potential of compromising their nutrient integrity by changing the optimal calorie-to-nitrogen ratio (Jeppesen & Mortensen, 1998).

Due to the lack of studies analyzing customized concentrations of formulas according to the absorptive capacity of the remaining intestine, a convenience set of concentrations of formulas and of additional energy supplements were analysed, providing a comprehensive list of combinations of energy and macronutrient densities. In spite of being slightly different from the manufacturers' recommended reconstitution, the chosen set of convenience concentrations includes currently used concentrations and it allows a direct comparison among different formulas. The chosen energy supplementations (10% and 20%) follow the current practice. We admit that further customization of both formula concentration and energy supplementation may be necessary in a clinical setting.

To summarize, a comprehensive list of osmolalities of elemental and semi-elemental formulas at the different concentrations currently used, enriched or not enriched with calories, is provided. This enables, at a glance, customization of the best combination of energy density, macronutrient densities, and P : E ratio, without exceeding the enteral osmolality suggested for infants with SBS.

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